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MUMMERT, STEPHANIE KANE				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary

Application No.

10/537,000

Applicant(s)

VOLLAND ET AL.

Examiner

STEPHANIE K. MUMMERT

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2008.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28, 29 and 31-54 is/are pending in the application.
4a) Of the above claim(s) 45 and 47-54 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 28, 29, 31-42 and 46 is/are rejected.
7) ☐ Claim(s) 43-44 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment filed on October 6, 2008 is acknowledged and has been entered. Claims 28 and 42 have been amended. Claims 1-27 and 30 have been canceled. Claims 28-29 and 31-54 are pending. Claims 45 and 47-54 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 28-29, 31-44 and 46 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made NON-FINAL in view of the newly applied references.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 31-42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oh et al. (US Patent 5,851,778; December 1998) in view of Lee et al. (J. Agr. Food Chem., 1999, vol. 47, p. 2766-2770) and Groopman et al. (PNAS, 1984, vol. 81, p. 7728-7731). Oh teaches a method of detection of target analytes using a capture member immobilized on a solid support through a trifunctional linker and detection of fluorescence (Abstract).

With regard to claim 28, Oh teaches a method for detection of an analyte a in a fluid sample, comprising the following steps:

- 1) saturating a solid support comprising, on at least part of its surface, at least one trifunctional reagent (tripod Y) (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as “the tridentate members operate pursuant to certain steric properties”; see Figure 11, where the space molecule is attached to a solid support; see also Example 7 and 8) comprising the following three functional poles:
 - i) a luminescent group (L) (Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label); see also isoluminol proximity label on the solid support);
 - ii) a molecule (B) selected from the group consisting of the analyte a, an analog of the analyte a or a fragment of the analyte a, which can non-covalently and reversibly bind a receptor specific for the analyte (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample); and
 - iii) a function that provides attachment of the trifunctional reagent to the surface of the solid

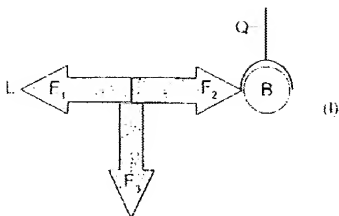
support (see Figure 11, where the spacer tridentate molecule is attached to a solid support; see also Example 7 and 8);

2) bringing the solid support obtained in step 1) into contact with a fluid sample that may comprise the analyte to be detected (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample; see col. 39, 'assay for analyte' heading, lines 8-20).

With regard to claim 33, Oh teaches an embodiment of claim 28, wherein the fluid sample consists of water, a liquid biological medium, or a liquid medium comprising dissolved gaseous molecules or molecules originating from solid samples (col. 39, lines 8-10, where the sample is a liquid sample comprising analyte).

With regard to claim 34, Oh teaches an embodiment of claim 28, wherein the intensity of the signal emitted during step 3) is determined by a luminescence detector (col. 39, line 8-15, where the sample is assayed using a luminometer, which detects luminescence).

With regard to claim 35, Oh teaches an embodiment of claim 28, wherein the complex C formed at the end of the saturation in 1) is selected from the group consisting of complexes of formula (I) below:



wherein:

- the arrows represent the structure of the backbone of the tripod Y, which is a linker arm consisting of a peptide, nucleotide or glucoside chain or of a saturated or unsaturated, linear or branched hydrocarbon-based chain; the chains being optionally substituted, interrupted and/or ended with one or more hetero atoms, such as N, O or S, and/or with one or more amino acids, and comprising three reactive chemical functions F_1 , F_2 and F_3 (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as "the tridentate members operate pursuant to certain steric properties"; see Figure 11, where the space molecule is attached to a solid support; see also Example 7 and 8; see also col. 18, lines 51-63);

the molecule (B) being covalently bonded to the tripod Y by the reactive chemical function F_2 (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample; see Example 4, where the details of the functional groups are provided);

- L represents a luminescent group covalently bonded to the tripod Y by the reactive chemical function F1 (Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label));
- F3 represents a reactive chemical function that can allow the attachment of the tripod Y to the surface of the solid support (Figure 11, Example 8, the tripod is attached to the solid support and comprises functional groups for attachment; see col. 18).

With regard to claim 36, Oh teaches an embodiment of claim 35, wherein the functions F1, F2 and F3, independently of one another, provide:

- i) either a direct linkage via a corresponding chemical function present on the luminescent compound, the molecule (B) or the solid phase (Figure 11, Example 7 and 8, where the tripod/tridentate is attached to the solid support and comprises functional groups for attachment; see col. 18 and Example 4, 'attachment of third tridentate member' where the tridentate comprises amine functional groups associated with the lysine based spacer);
- ii) or an indirect linkage, and in this case, the linkage is carried out by coupling, to at least one of the functions F1, F2 and/or F3, a molecule M1 forming a complex with a molecule M2 attached beforehand to at least part of the surface of the solid phase, to the molecule (B) and/or to the luminescent group (Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label)).

With regard to claim 37, Oh teaches an embodiment of claim 35, wherein the functions F1, F2 and F3, which may be identical or different, are selected from the group consisting of: thiols; amines; alcohols; acid functions; esters; isothiocyanates; isocyanates; acylazides; sulfonyl chlorides; aldehydes; glyoxals; epoxides; oxiranes; carbonates; imidoesters; carbodiimides;

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maleimides; nitriles; aziridines; acryloyl; halogenated derivatives; disulfide groups; phosphorus-containing groups; diazo; carbonyldiimidazole; hydrazides; arylazides; hydrazines; diazirines; magnesium compounds; lithium compounds; cuprates; zinc compounds and unsaturated systems (see col. 18 and Example 4, 'attachment of third tridentate member' where the tridentate comprises amine functional groups associated with the lysine based spacer).

With regard to claim 38, Oh teaches an embodiment of claim 37, wherein the functions F1, F2 and F3 are selected from the group consisting of amine functions of formulae R- NH₂, R- NH-, (R)₃-N, R-NH-OR and NH₂-OR; alcohol functions R-OH; and halogenated groups of formula R-X with X representing a halogen atom; it being understood that, in tile formulae, R represents an alkyl, aryl, vinyl or allyl radical (see col. 18 and Example 4, 'attachment of third tridentate member' where the tridentate comprises amine functional groups associated with the lysine based spacer).

With regard to claim 39, Oh teaches an embodiment of claim 28, wherein the luminescent group is selected from the group consisting of fluorescein and its derivatives; rhodamine and its derivatives; diaminidophenyl indo; acridine; fluorescent dyes with reactive amines; eosin; and erythrosine (Figure 11, Example 8, where DNP is labeled with a anti-DNP antibody labeled with fluorescein (proximity label)).

With regard to claim 40, Oh teaches an embodiment of claim 28, wherein the receptor is selected from the group consisting of antibodies in whole, fragmented or recombinant form, biological receptors, nucleic acids, peptide nucleic acids, lectins, transporter proteins, chelates and synthetic receptors (Figure 11, Example 8, where theophylline analog/analyte is present on the structure and where the assay measures the presence of theophylline in a sample; see claim

18, where the modulating member comprises an analyte or analyte analog and the binding partner comprises an antibody).

With regard to claim 41, Oh teaches an embodiment of claim 28, wherein the receptor exhibits greater affinity for the analyte a than for the molecule (B) (Figure 11, Example 8, where theophylline analog/analyte is present on the structure and where the assay measures the presence of theophylline in a sample; see claim 18, where the modulating member comprises an analyte or analyte analog and the binding partner comprises an antibody).

With regard to claim 46, Oh teaches a method for continuous heterogeneous-phase detection of an analyte a in a fluid sample, comprising detecting the analyte a in a fluid sample with at least one complex C of formula (I) (Figure 11, Example 8, where theophylline analog/analyte is present and where the assay measures the presence of theophylline in a sample).

Regarding claim 28, 33-41 and 46, Oh does not teach that the analyte specific receptor was labeled with a compound that quenches luminescence. Lee teaches a homogeneous method of immunoassay for the detection of an analyte, however, Lee also teaches that the interaction and competition between a quenched reporter and a luminescent pseudo-antigen results in detection of the target analyte (Abstract).

With regard to claim 28, Lee teaches a receptor for analyte a, the receptor being labeled with a compound (Q) that quenches the luminescence of the group L (p. 2768, 'fluorescence excitation transfer measurements' heading; p. 2767, col. 1, where when the antibody/receptor binds to labeled antigen/analyte, fluorescence quenching occurs; p. 2767, where the antibody/receptor is labeled with a quencher, Q);

3) measuring the intensity of the signal emitted by the group L, which is proportional to the amount of analyte a present in the fluid sample (p. 2768, 'fluorescence excitation transfer measurements' heading; p. 2767, col. 1, where when the antibody/receptor binds to labeled antigen/analyte, fluorescence quenching occurs, when sample containing analyte is added unlabeled analyte/antigen competes for the receptor/antibody site and the amount of fluorescence quenching is reduced in proportion to the concentration of analyte in the sample); and wherein step 3) and step 4) are carried out continuously (p. 2768, 'fluorescence excitation transfer measurements' heading).

With regard to claim 35, Lee teaches components of the structure of complex C, comprising:

- the receptor for analyte a being labeled with a compound Q (p. 2768, 'fluorescence excitation transfer measurements' heading; p. 2767, col. 1, where when the antibody/receptor binds to labeled antigen/analyte, fluorescence quenching occurs; p. 2767, where the antibody/receptor is labeled with a quencher, Q);
- Q represents a compound that quenches the luminescence of the group L (p. 2768, 'fluorescence excitation transfer measurements' heading; p. 2767, col. 1, where when the antibody/receptor binds to labeled antigen/analyte, fluorescence quenching occurs; p. 2767, where the antibody/receptor is labeled with a quencher, Q).

With regard to claim 42, Lee teaches an embodiment of claim 28, wherein the quenching compound (Q) is selected from the group consisting of rhodamine and its derivatives, the fluorescent compounds mentioned in claim 12, and nonfluorescent molecules (p. 2767, col. 2,

'labeling of Ab' heading, where the antibody is reacted through an amine reactive reagent, TMR-SE; which is a rhodamine derivative).

Regarding claim 28, while Lee teaches regeneration of the assay, Lee does not teach a solid support. Regarding claim 31-32, while Oh teaches a solid support, Oh is not explicit regarding the details of the solid support. Groopman teaches regeneration of solid supports useful in immunoassays (Abstract).

With regard to claim 28, Groopman teaches 4) regenerating the solid support by bringing the solid support into contact with the receptor-Q (p. 7730, col. 2, where the solid support was regenerated using a wash; see also p. 7731, col. 1).

With regard to claim 31, Groopman teaches an embodiment of claim 28, wherein the solid support is selected from the group consisting of glasses, plastics, ceramics, metals and metalloids (p. 7729, col. 2, where the solid support comprised an affinity column).

With regard to claim 32, Groopman teaches an embodiment of claim 28, wherein the solid support is in the form of a tube, a capillary, a plate or a bead (p. 7729, col. 2, where the solid support comprised an affinity column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the competitive quenched format of detection taught by Lee to the solid phase receptor based format of immunoassay taught by Oh to arrive at the claimed invention with a reasonable expectation for success. In Oh, proximity assays are carried out between a proximity label associated with a small molecule ligand, DNP, which is very similar to the receptor for the analyte, labeled with a quencher, as claimed (see Figure 11, Example 8). Oh differs from the instant claims because the receptor for the analyte is not labeled and the end

resulting signal is achieved in a different way. First, it would have been obvious in view of the combination of proximity labels between a small molecule ligand and a labeled receptor. However, it is also noted that Lee teaches a homogeneous assay where a luminescent group is attached to the molecule B or analyte and where the proximity between the label and quencher as taught by Lee achieves a format wherein the support is quenched prior to assay, followed by competition with an unlabeled analyte overcoming the quenching leading to increase in signal which is proportional to the amount of analyte in the sample. Therefore, it would have been *prima facie* obvious to achieve the method of the instant invention through a combination of Oh and Lee. As taught by Lee, "when sample Ag is introduced into solution, competition for the Ab binding sites occurs between the nonlabeled sample Ag and labeled Ag, and the amount of fluorescence quenching will be reduced in proportion to the concentration of nonlabeled Ag" (p. 2767, col. 1). Furthermore, while Lee is a homogeneous assay and Oh teaches a heterogeneous assay, the two complimentary methods of proximity assay incorporating the interaction between fluorescent labels and quenchers, the labeling and detection format of Lee is applicable to both homogeneous and heterogeneous assays. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the competitive quenched format of detection taught by Lee to the solid phase receptor based format of immunoassay taught by Oh to arrive at the claimed invention with a reasonable expectation for success.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Lee and Oh to include the solid supports as taught by Groopman and the regeneration of the support as taught by Groopman to arrive at the claimed invention with a reasonable expectation for success. As taught by Groopman, "the

antibody column was regenerated by washing the column with Pi/NaCl (pH 7.4); to date, we have used and regenerated this column more than 25 times with no apparent loss of activity” (p. 7730, col. 2). Groopman also teaches, “we have also found that when this antibody is bound to a solid-phase matrix, a reusable column can be prepared that selectively isolates aflatoxins from complex mixtures, such as urine, serum and milk” (p. 7731, col. 2). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Lee and Oh to include the solid supports as taught by Groopman and the regeneration of the support as taught by Groopman to arrive at the claimed invention with a reasonable expectation for success.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable Oh et al. (US Patent 5,851,778; December 1998) in view of Lee et al. (J. Agr. Food Chem., 1999, vol. 47, p. 2766-2770) and Groopman et al. (PNAS, 1984, vol. 81, p. 7728-7731) as applied to claims 28, 30-42 and 46 above and further in view of Plowman et al. (Analytical Chemistry, 1999, vol. 71, p. 4344-4352). Oh teaches a method of detection of target analytes using a capture member immobilized on a solid support through a trifunctional linker and detection of fluorescence (Abstract).

Regarding claim 29, Oh teaches tripods Y (col. 14, lines 14-18, where the trifunctional reagent or tripod is referred to as “the tridentate members operate pursuant to certain steric properties”; see Figure 11, where the space molecule is attached to a solid support; see also Example 7 and 8). However, neither Oh nor Lee teaches multiple types of tripods or the detection of multiple analytes.

With regard to claim 29, Plowman teaches an embodiment of claim 28, wherein several types of tripods Y that differ from one another through the nature of the molecule (B) that they comprise are attached to distinct and known zones of the solid support (Abstract, Figure 1, Table 2, where the method is applied to the detection of multiple analytes and therefore different formats of the reagent attached to the solid support).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the detection of multiple targets as taught by Plowman to the method of detection taught by Oh and Lee to arrive at the claimed invention with a reasonable expectation for success. As taught by Plowman, "Multiple analyte immunoassay (MAIA) results for two sets of three different analytes, one employing polyclonal and the other monoclonal capture antibodies, where compared with the results for identical analytes performed in a single analyte immunoassay (SAIA) format" (Abstract). Plowman therefore teaches the detection and analysis of multiple analytes in an immunoassay format similar in practice to the methods of Oh and Lee. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the detection of multiple targets as taught by Plowman to the method of detection taught by Oh and Lee to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments with respect to claims 28-29, 31-44 and 46 have been considered but are moot in view of the new ground(s) of rejection.

Pertinent Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Miyazaki et al. (US Patent 5,229,302; July 1993) teaches a fluorescence immunoassay wherein the presence of analyte increases fluorescence that was previously quenched (Abstract). Ballerstadt et al. (Analytica Chimica Acta, 1997, vol. 345, p. 203-212) teaches a fluorescence quenching affinity assay for the detection of lectins (Abstract).

Conclusion

Claims 43 and 44 are free of the prior art. A thorough search of the prior art of the specific elected structure, Y2 and Y'2 was conducted and there was no disclosure in the prior art of the specifically elected structure. While the prior art teaches multifunctional reagents, the specific structure is not disclosed and would not have been an obvious structure based on the more general teachings in the prior art.

Claims 43 and 44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 28-42 and 46 stand rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/
Examiner, Art Unit 1637

SKM